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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/595,108	02/17/2006	Murray D. Bailey	13-0128	2759

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EXAMINER	
ROBINSON, BINTA M	

ART UNIT	PAPER NUMBER
1625	

MAIL DATE	DELIVERY MODE
11/13/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/595,108	BAILEY ET AL.	
	Examiner	Art Unit	
	BINTA M. ROBINSON	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *Applicant's arguments filed 2/25/08*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20,23 and 25-27* is/are pending in the application.

4a) Of the above claim(s) *20 and 23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-19 and 25-27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Detailed Action

The 102 (e) rejection over US PG Pub 2005/0020503 as well as the obvious double patenting rejection and 103 (a) rejection over US PG Pub 2005/0020503 have been rendered moot in light of applicant's comments and amendments. Claims 20, 23 are withdrawn from consideration as being drawn to a non-elected invention.

(modified rejection)

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-19, 25-27 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for using the compounds of formula I with Y equal to H, R3 equal to isobutyl, R1 equal to H, n equal to 1, R4 equal to alkyl, R6 is equal to alkyl, m is equal to 1, R2 is equal to  , R5 equal to (C1-C10) alkyl optionally substituted with –COO(C1-6)alkyl or (C3-7)cycloalkyl, does not reasonably provide enablement for using compounds of formula I with Y, R3, R1, n, R4, R5, R6, m, and R2 equal to all other moieties claimed other than those stated above. Claim 27

is also enabled for intermediates, only when Y is equal to H, R3 is equal to isobutyl, R1 is equal to H, n equals 1, R5 equals (C1-C10) alkyl optionally substituted with –COO(C1-6)alkyl or (C3-7)cycloalkyl, R2 is equal to  , but is not enabled for intermediates when these radicals equal all other moieties claimed other than those stated above to be enabled. The specification does not enable any skilled pharmacologist or physician to use the invention commensurate in scope with these claims. The factors to be considered in making an enablement rejection have been summarized above.

a) Determining if any particular claimed compounds with Y, R3, R1, n, R4, R6, m, and R2 equal all other moieties claimed other than those stated to be enabled above would be active would require synthesis of the substrate and subjecting it to testing with Applicants' NS3-NS4A Protease Assay, Cell-based luciferase reporter HCV RNA Replication Assay, specificity assays. Considering the large number of compounds to be made this is a large quantity of experimentation. b) The direction concerning the claimed compounds is found in page 97 through 136, which merely states Applicants' intent to make and use such compounds. c) In the instant case, none of the working examples contains any radicals

Y, R3, R1, n, R4, R6, m, and R2 equal to all other moieties claimed other than those stated to be enabled above. d) The nature of the invention is inhibition of NS3 protease and treatment of human diseases with Applicants' compounds. This involves physiological activity. The nature of the invention requires an understanding of the NS3 protease, the binding activity of small ligands to that protease, and the ability of those compounds to inhibit it. In view of the unpredictability of receptor binding activity and claimed divergent substituents with varied polarity, size, and polarisability, the skilled physician would indeed question the inclusion of such diverse rings, commensurate in scope with these claims. Also see the MPEP § 2164.03 for enablement requirements in the structure sensitive arts of pharmacology and medicinal chemistry.

e) There is no reasonable basis for the assumption that the myriad of compounds embraced the present formula (I) will all share the same biological properties. For example, R20 equal to phenyl or napthyl will not have the same properties as a compound of formula with R20 equal to thienyl or furyl, or other heteroaryl rings. There is no reasonable basis for the assumption that the myriad of compounds embraced the present formula (III) will all share the same biological properties. The diverse

claimed compounds are chemically non-equivalent and there is no basis in the prior art for assuming in the non-predictable art of pharmacology that structurally dissimilar compounds will have such activity, *In re Surrey* 151 USPQ 724 (compounds actually tested which demonstrated the asserted psychomotor stimulatory and anti-convulsant properties were those having the 3,4-dichlorophenyl substituent at the 2-position on the thiazolidone nucleus not sufficient for enablement of any heterocyclic radical at the same position). *In re Fouche*, 169 USPQ 429 at 434 (a Markush group including both aliphatic and heterocyclic members not enabled for the use of those compounds within the claim having heterocyclic moieties.) *In re CAVALLITO AND GRAY*, 127 USPQ 202 (claims covering several hundred thousand possible compounds, of which only thirty are specifically identified in appellants' application, not enabled unless all of the thirty specific compounds disclosed had equal hypotensive potency because that fact would strongly indicate that the potency was derived solely from the basic structural formula common to all of them. A wide variation in such potency would suggest that it was due in part to the added substituents and might be eliminated or even reversed by many of the possible substituents which had not been tried.)

f) The artisan using Applicants' invention to treat diseases with the claimed compounds would be a physician with a MD degree and several years of experience. He would be unaware of how to predict *a priori* how a changing a heterocyclic ring would affect biological activity. In view of the divergent rings with varied basicity, steric hindrance, and polarisability, the skilled physician would indeed question the inclusion of such fused rings, commensurate in scope with these claims. g) Physiological activity, is well-known to be unpredictable, *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) (contrasting mechanical and electrical elements with chemical reactions and physiological activity). See also *In re Wright*, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993); *In re Vaeck*, 947 F.2d 488, 496, 20 USPQ2d 1438, 1445 (Fed. Cir. 1991). h) The breadth of the claims includes all of millions of compounds of formula (I). Thus, the scope is very broad. The present claims embrace various heterocyclic radicals, which are not art-recognized as equivalent. The specific compounds made are not adequately representative of the compounds embraced by the extensive Markush groups instantly claimed.

MPEP 2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the

specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here. Thus, undue experimentation will be required to practice Applicant s' invention.

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-19, 25-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent 7132504.

'504 teaches the genus of compounds as shown in Formula I, at claim 1, column 78, articles of manufacture containing this compound, and a process of making these compounds. The difference between the prior art compound, articles of manufacture, and a process of making and the instantly claimed compounds, articles of manufacture and a process of making is the teaching of a generic compound, articles of manufacture and a process of making this genus of compounds which overlaps with the subject matter of the instant genus of compounds, articles of manufacture and a process of making this genus. It would have been obvious to one of ordinary skill in the art to

select various known radicals within a genus to prepare structurally similar compounds, articles of manufacture and a process of making. Accordingly, the compounds, articles of manufacture and process of making are deemed unpatentable therefrom in the absence of a showing of unexpected results for the claimed compounds over those of the generic prior art compounds.

(New rejection)

1. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

2. Claims 1-19, 25 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 56-59 of copending Application No. 11766171. Although the conflicting claims are not identical, they are not patentably distinct from each other because the copending application

claims a genus of compositions which overlap in subject matter with the instant genus of compounds and compositions.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

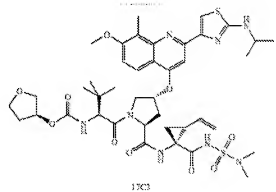
Copending application teaches the compositions containing a genus of compounds which overlap in subject matter with the instant genus of compounds and compositions. See claim 56. The difference between the copending composition and the instantly claimed compounds and composition is the teaching of a generic composition which overlaps in subject matter with a genus of compounds and compositions. It would have been obvious to one of ordinary skill in the art to select various known radicals within a genus to prepare structurally similar compounds and compositions. Accordingly, the compounds and compositions are deemed unpatentable therefrom in the absence of a showing of unexpected results for the claimed compounds and compositions over those of the generic compositions.

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

4. Claims 1-13, 15-19 are rejected under 35 U.S.C. 102(e) as being anticipated by anticipated by Llinas-Brunet et. al. (US 2007/0243166 A1).

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131. Llinas-



Brunet et. al. discloses the instant compound .

Response to Applicant's Remarks

Applicant's traverse the 112, first paragraph rejection alleging that the specification provides adequate teachings for one of ordinary skill in the art to make and use the claimed invention without undue experimentation. The applicants' assert that the PTO has not provided evidence or objective reasoning substantiating the allegation of the lack of enabling disclosure. However, the examiner disagrees. The examiner stated above that alternative members of the genus of compounds of formula I for example, wherein R2 equals phenyl or napthyl or furyl or thienyl are not obvious over one another and are not therefore expected to exhibit similar chemical properties.

The compounds presented in the declaration as being tested in the HCV RNA replication assay are not sufficiently representative of the genus being claimed.

5. The 103 (a) rejection over US Patent 7132504 is traversed by the applicant because the applicant alleges that the proviso overcomes the art. The applicant alleges that the compounds as defined by the art are those wherein the B group is –C(=O)-O-alkyl with alkyl being methyl or tert-butyl. However, the B group is not only limited to this moiety. B can also be -C(=O)-O(C3-7)cycloalkyl which also renders obvious the claims.Any inquiry concerning this communication or earlier communications from the examiner should be directed to Binta M. Robinson whose telephone number is (571) 272-0692. The examiner can normally be reached on M-F (9:30-6:00).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Binta M. Robinson whose telephone number is (571) 272-0692. The examiner can normally be reached on M-F (9:30-6:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached on 571-272-0670.

A facsimile center has been established. The hours of operation are Monday through Friday, 8:45 AM to 4:45 PM. The telecopier numbers for accessing the facsimile machine are (703)308-4242, (703305-3592, and (703305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571)272-1600.

/Binta M Robinson/
Examiner, Art Unit 1625
/Janet L. Andres/

Supervisory Patent Examiner, Art Unit 1625